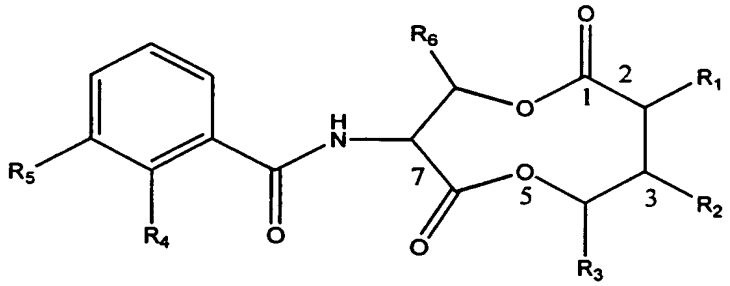
WHAT IS CLAIMED IS:

1. An agent which modulates apoptosis by binding to a Bcl-2 family member protein and preferentially induces apoptosis in a cell which over-expresses the Bcl-2 family member protein.

2. The agent of claim 2, wherein the Bcl-2 family member protein is Bcl-2 or Bcl-x_L.

3. The agent of claim 1 in which the agent is of the following formula and an absolute configuration of [2R, 3R, 4S, 7S, 8R]:



(II)

wherein R_1 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_2 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_3 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_4 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, or a substituted alkyl group; and

R_5 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-alkylamine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group; and

R_6 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

with the proviso that the agent is not antimycin $A_{0\,(a-d)}$, A_1, A_2, A_3, A_4, A_5, A_6, kitamycin A or B, urauchimycin B, deisovaleryl blastomycin, dehexyl-deisovaleryloxy antimycin A, 2-methoxy ether antimycin A_3, deformyl antimycin A_1 or A_3, antimycin diacetate A_3, deformyl antimycin triacetate A_3, deformyl-N-acetyl antimycin A_3, or deformyl-N-bromo-acetyl antimycin A_3.

4. The agent of claim 3, which is

(a) 3-methylbutanoic acid 3-[[3-(acetylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(b) 3-methylbutanoic acid 8-butyl-3-[[3-(acetylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(c) 3-methylbutanoic acid 3-[2-hydroxybenzoylamino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(d) 3-methylbutanoic acid 8-butyl-3-[[2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(e) 3-methylbutanoic acid 3-[[3-amino-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(f) 3-methylbutanoic acid 8-butyl-3-[[3-amino-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(g) 3-methylbutanoic acid 3-[[3-(propionylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(h) 3-methylbutanoic acid 8-butyl-3-[[3-(propionylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(i) 3-methylbutanoic acid 3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2-methyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(j) 3-methylbutanoic acid 8-butyl-3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-2-methyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(k) 3-hydroxyl 3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(l) 3-hydroxyl 8-butyl-3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(m) 3-methylbutanoic acid 3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-8-methyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(n) 3-methylbutanoic acid 8-butyl-3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester; or

(o) the compound of formula VII.

5. The agent of claim 1, wherein the agent binds to the hydrophobic pocket of the Bcl-2 family member protein formed by the BH1, BH2 and BH3 domains of the protein.

6. The agent of claim 1, wherein the agent exhibits reduced binding affinity for cytochrome B.

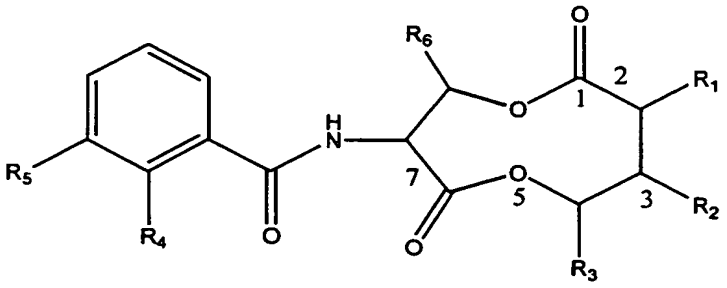
7. The agent of claim 1, further comprising a pharmaceutically acceptable carrier.

8. The agent of claim 1, wherein the agent is a biologically active derivative of antimycin A_1 or A_3.

9. The agent of claim 1 for use in treating an apoptosis-associated disease in a subject in need thereof.

10. The agent of claim 1 for use in inducing apoptosis in a cell in a subject.

11. An apoptotic agent that modulates apoptosis by binding to a Bcl-2 family member protein and preferentially inducing apoptosis in a cell that over-expresses the Bcl-2 family member protein, the agent having the following formula II,



(III)

having an absolute configuration of [2R, 3R, 4S, 7S, 8R], and comprising at least a first and a second chemical modification, the first chemical modification decreasing the affinity of the agent for cytochrome B, wherein the first chemical modification is selected from the following:

R_4 is hydrogen, a C_1-C_8 linear or branched alkane, a C_1-C_8 hydroxyalkane, or a substituted alkyl group; and

R_5 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_3-C_8 di- or tri-alkylamine, a C_1-C_8 carboxylic acid, a C_2-C_8 amide, or a substituted alkyl group;

and the second chemical modification is selected from the following:

R_1 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_2 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_3 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group; and

R_6 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group.

12. The agent of claim 11, further comprising a pharmaceutically acceptable carrier.

13. The agent of claim 11 for use in treating an apoptosis-associated disease in a subject in need thereof.

14. The composition of claim 11 for use in inducing apoptosis in a cell in a subject.

15. A method for identifying an agent which modulates apoptosis of a cell by binding to the hydrophobic pocket of an anti-apoptotic Bcl-2 family member protein formed by the BH1, BH2 and BH3 domains of the protein, comprising:

a) admixing a candidate compound with a cell which over-expresses the anti-apoptotic Bcl-2 family member protein;

b) admixing the candidate compound with a control cell which does not over-express the anti-apoptotic Bcl-2 family member protein; and

c) determining whether the candidate compound modulates the activity of the anti-apoptotic Bcl-2 family member protein to produce a physiological change in the cell which over-expresses the anti-apoptotic Bcl-2 family member protein indicative of apoptosis, but does not produce a substantial physiological change in the cell which does not over-express the anti-apoptotic Bcl-2 family member protein.

16. The method of claim 15, wherein the anti-apoptotic Bcl-2 family member protein is Bcl-x_L or Bcl-2.

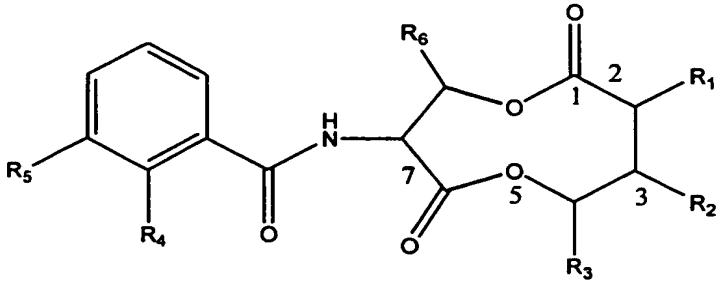
17. The method of claim 15, wherein the physiological change indicative of apoptosis is cell shrinkage, chromosome condensation and migration, mitochondrial swelling, or disruption of mitochondrial transmembrane potential.

18. The method of claim 17, wherein the cellular change comprises disruption of mitochondrial transmembrane potential.

19. The method of claim 15, wherein the cell that over-expresses the anti-apoptotic Bcl-2 family member protein is transfected with a gene which encodes the anti-apoptotic Bcl-2 protein.

20. A method for treating a subject having an apoptosis-associated disease, comprising administering to the subject a therapeutically effective amount of an antimycin or an antimycin derivative.

21. The method of claim 20 wherein the antimycin or antimycin derivative is of the following formula, and having an absolute configuration of [2R, 3R, 4S, 7S, 8R]:



(II)

wherein R_1 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_2 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_3 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_4 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 carboxylic acid, or a substituted alkyl group;

R_5 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-alkylamine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group; and

R_6 is hydrogen, a C_1-C_8 linear or branched alkane, hydroxyl, a C_1-C_8 hydroxyalkane, amino, a C_1-C_8 di- or tri-amine, a C_1-C_8 amide, a C_1-C_8 carboxylic acid, or a substituted alkyl group.

22. The method of claim 21, wherein the antimycin derivative is 2-methoxy ether antimycin A or A_3.

23. The method of claim 21, wherein the antimycin derivative is:

(a) 3-methylbutanoic acid 3-[[3-(acetylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(b) 3-methylbutanoic acid 8-butyl-3-[[3-(acetylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(c) 3-methylbutanoic acid 3-[2-hydroxybenzoylamino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(d) 3-methylbutanoic acid 8-butyl-3-[[2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(e) 3-methylbutanoic acid 3-[[3-amino-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(f) 3-methylbutanoic acid 8-butyl-3-[[3-amino-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(g) 3-methylbutanoic acid 3-[[3-(propionylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(h) 3-methylbutanoic acid 8-butyl-3-[[3-(propionylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(i) 3-methylbutanoic acid 3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2-methyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(j) 3-methylbutanoic acid 8-butyl-3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-2-methyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(k) 3-hydroxyl 3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-8-hexyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(l) 3-hydroxyl 8-butyl-3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(m) 3-methylbutanoic acid 3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-8-methyl-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester;

(n) 3-methylbutanoic acid 8-butyl-3-[[3-(formylamino)-2-hydroxybenzoyl]amino]-2,6-dimethyl-4,9-dioxo-1,5-dioxonan-7-yl ester; or

(o) the compound of formula VII.

24. The method of claim 20, wherein the subject is human.

25. The method of claim 20, further comprising administering a pharmaceutical carrier.

26. The method of claim 20, wherein the administration is intravenous, subcutaneous, intramuscular, intradermal, transdermal, intrathecal, intracerebral, intraperitoneal, epidural or oral.